Comments of Mr. Jay R. Schrand.

Comment 1:

Part B: Health Effects
New developments since the last evaluation in 1997:

Comment:

Missing from all studies on the purported harmful effects of tobacco use on morbidity and mortality, is an analysis of the confounding influence of exposure to Adverse Childhood Experiences (ACE's) and of the stress of the Anti-tobacco program itself.

Background: In this series of studies, ACE's, being exposed to child abuse or household dysfunction had a graded influence on a host of risky behaviors including tobacco use, alcohol and drug abuse, paternity and teen pregnancy, depression, attempted suicide and eating disorders. ACE's also have an independent, graded effect on mortality. Feletti acknowledges that Nicotine may have beneficial psychoactive effects regulating affect, and mood, consequences of depression. Nicotine is well known for reducing stress and increasing attention span. Does tobacco use really cause stress related heart disease? Or is tobacco use simply a marker for stress? Unfortunately, the article, does not present the intercorrelations between ACE's, tobacco use and mortality. This would be a difficult model, but is still significant by its absence. We would not expect that the stress of exposure to ACE's to effect (non-stress related) cancers of the respiratory system. However, stress in implicated in <u>every</u> other illness attributed to tobacco use.

Response:

Most epidemiological studies of the adverse health effects of ETS adjust the studies for confounders related to socioeconomic status or SES. Since stress and resulting behavioral consequences is strongly influenced by poverty, then appropriate confounder adjustment for SES is likely to reduce any effects of what the comment refers to as ACES, assuming these originate from poverty. Also, the comment ignores the fact that there are a number of toxic constituents of tobacco smoke that provide a biological plausibility for adverse health effects noted including particulate matter, CO, aldehydes, a host of carcinogens, and so on.

Comment 2:

The confounding influence of ACE's as it applies to maternal smoking and Fetal Growth and Preterm Delivery (FG&PtD), including BW, LBW, IUGR, SGA.

Several studies have included some of the measures of stress: adverse adult life experiences, trait anxiety, current stress, and domestic violence during pregnancy. However, none have measured the entire range to include ACE's.

A case control study of partner abuse and LBW (Campbell 1999) found that < 15 pound weight gain, spousal abuse and smoking during pregnancy was associated with LBW in full term infants, but only < 15 pound weight gain was related in preterm infants. Smoking was not included in the final adjusted model(assuming that it did not influence the final model). Stress (Daily Hassles Scale) was associated with abuse, but not LBW. The author suggests that "Abuse may be one of a cluster of difficult life experiences that affect birth weight"

One interesting (n=1861) Urban prospective study (Orr 1996) of psychosocial stressors and LBW found that African Americans have a higher rate of LBW and correlation with Moderate/High Stressors and hypertension, whereas the Caucasian population has a lower rate of LBW which is more highly correlated with hypertension, low pre-pregnancy weight, smoking and drug use.

The prevalence of high levels of stressors and established risks (including smoking) in this study was similar in both races. Yet, the risk (odds ratio) for smoking is 6.89 for Caucasians and 1.57 in African Americans. Smoking is a greater risk factor for LBW for Caucasians than it is for African Americans? How can this possibly be?

Table 1

	Caucasian n= 428 LBW= 32		**African-American** n=1433 LBW=156	
	P-value	Odds Ratio	P-value	Odds Ratio
Moderate/High Stressors	.10	.48	.03	1.52
Low Pre-pregnancy Weight	.17	2.29	.005	2.13
Hypertension	.002	15.11	.02	2.93
Smoking	.002	6.89	.03	1.57
Drug Use	.05	2.95	.18	1.48

Table 2

	Caucasian	**African-American**
LBW rate (1990/1995)	5.7/6.22	13.25/13.13
Smoking rate (1990/1995)	23.5/23.4%	20.8/23.5
Decrease in Smoking rate (1990/1995)	.4%	- 13%
Smoking/preg rate (1990/1995)	19.4/15.0%	15.9/10.6%
Decrease in Smoking/preg rate (1990/1995)	22.6%	33.3%

Health, United States, 2003 Trend Tables (tables 10,12,59)
http://www.cdc.gov/nchs/products/pubs/pubd/hus/03hustop.htm

From 1990 to 1995 smoking rates in the US for African American females increased, pregnant African American females decreased 33% as compared to 22.6% for Caucasians(Table 2). One would have to assume that pregnant females in the US were especially targeted with anti-smoking programs, with African American females getting the extra heavy dose. During this time, there was no significant decrease in the rate of LBW(Table 2). Recognizing that those who do quit are the easy ones, with a low Nicotine Tolerance score and associated risks for tobacco related illnesses anyway, one would have to question the utility of the anti-smoking program in the first place.

The author speculates that "a minority group, traditionally suffering exploitation and discrimination, may react differently to stressors than their Caucasian counterparts."

Indeed, this may be because of an increase in genetic susceptibility over several generations. It may also be because of the (cumulative) effect of stressors that were not identified in the Prenatal Social Environment Inventory (PSEI) survey instrument. The author made it a point to include measures of chronic stressors (during the past 12 months) that were unique to African American culture. This apparently lowered their odds ratio for smoking to a paltry 1.57 that, while still "significant", is still highly subject to unknown confounding factors, such as ACE's, partner abuse, and exposure to heavy doses of anti-tobacco messages.

Stress can be mitigated by periods of down time: social support, security, economic prosperity, and sated sleep. For black females, typically raising families alone, this is especially problematic. Societies help too often involves sending critical messages, marginalizing those who appear outside the norm. So, we have an at risk population that has suffered exploitation, and discrimination because they are black and female and now because they smoke. We as a society have come so far, and yet, still such a long distance to go.

Response:

The comment brings up a number of important differences between Caucasians and African-Americans in terms of societal stress factors and stress levels. These important factors may indeed influence birth outcome. However, there are a number of large studies that demonstrate that ETS exposure can influence birth outcome that adjust for SES. Any confounder adjustment will not be perfect, but the association is still present after adjusting for these confounders.

Comment 3:

As it applies to studies of pregnant non-smoking spouses of smokers (ETS):

Refer to Chapter 3. Developmental Toxicity - 1. Perinatal Manifestations

3.2 Fetal Growth and Preterm Delivery

None of the studies of ETS and FG&PtD have included ACE's in the parents. Those who are exposed to ACE's are more likely to smoke. The presence of measures of ETS (Cotinine) in the mother (or child) even though she does not actively smoke may be a marker for exposure to ACE's in the mother or because of assortive mating(discussed below), in the biological father who smokes. Either biological parent may transfer the genetic risk for FG&PtD. The father, because he smokes and is at increased risk for ACE's, may also be at increased risk for spousal abuse during pregnancy, another risk factor for FG&PtD. Paternity is a marker for ACE's also an issue. The same would apply to biological relatives living in the home.

Response:

The point of this comment is not clear. The presence of cotinine is a chemical marker for recent ETS exposure, not for distant exposure.

Comment 4:

As it applies to studies of infants of non-smoking spouses of smokers (ETS):

Refer to Chapter 4. Developmental Toxicity - II. Postnatal Manifestations

4.1 Sudden Infant Death Syndrome (SIDS)

None of the studies of ETS and SIDS have included ACE's in the parents. The same analysis as above applies.

Response:

The studies of SIDS have been well-conducted and do include correction for SES, maternal education and a number of other important risk factors. The comment does not provide a method to include "ACES" as a confounder in a meaningful way in an epidemiological study. For example, how would one determine a method to measure "ACES"?

Comment 5:

Animal Models

Animal are not reliable models of human exposure. In all studies that I am aware of, animals do not select to use tobacco (nicotine). Humans do choose actions to preserve and enhance life.

Tobacco has been in use for 2000 years. Those who smoke are not dying off in their 20's.

Response:

Comment noted. We disagree that animals are not meaningful models of toxicological effects. The statement is contrary to a large body of evidence. The toxicological effects of a large number of substances including nicotine have been elucidated in animal models, and are clearly applicable to humans.

Comment 6:

Biomarkers of Exposure

Is it the Nicotine? Well, as it turns out, there is no Nicotine in ETS. Cotonine, one of the metabolites of Nicotine can be measured as a proxy. Is it Benzene or Vinyl Chloride (Table 7-4D). Both are identified as carcinogens by the IARC. There has not been any identification as to exactly which of the purported harmful constituents causes the specific illnesses or conditions associated with exposure to ETS. In fact, if the particular constituent could be identified, the manufacturing process could be changed to eliminate the harmful constituent.

There is no safe exposure? If you apply this idea to the extreme, it implies that <u>any</u> exposure to ETS is harmful. In other words, a person smoking in Los Angeles could theoretically effect the health of someone in Washington, DC. Of course, this is ludicrous. Unless the specific constituent of tobacco is identified, and the exact amount and time exposure required (not just the risk) to cause cancer, then it would be improper to regulate it as toxic.

Response:

The commenter is misinformed as to the relationship between nicotine and cotinine. As explained in Part A of the document, nicotine does occur in tobacco smoke, whether mainstream, sidestream or environmental. Cotinine is formed by metabolic conversion in the body of a smoker or ETS exposed, and is excreted in the urine: it is not a component of the smoke.

There are clearly a number of chemicals in ETS that are pharmacologically and toxicologically active. It is not necessary to ascertain which chemicals are the most important actors in producing the effects noted in epidemiological studies. It is not clear to date which are the most important lung carcinogens in tobacco smoke and which interactions among those carcinogens are the most critical, yet it is quite clear from epidemiological studies that cigarette smoking causes lung cancer.

Comment 7:

Assortive Mating

A recent letter (Willensen 2003) commenting on a study (Price 2003) of spousal similarities found that "assortative mating should not be hastily dismissed as a cause for spouse similarities in disease". Part of the risk for cancer is genetic susceptibility. The spouse, through assortment for these factors (including ACE's) is based on similarity at the time dating began, is likely to have an increased risk for these same factors.

Response:

Since the spouse is not genetically related to their mate, the point in this comment regarding genetic susceptibility is not clear. While humans tend to marry within their social strata, and disease rates are related to poverty, it is likely that there are factors in common for diseases that are related to lifestyle, income, and so on. However, since the majority of epidemiological studies account for lifestyle factors primarily by looking at SES (and related correlated factors like education), then confounding by these factors in studies of ETS (or active smoking for that matter) is diminished.

Comment 8:

The social effects of ACE's, stress and the Anti-tobacco program

ACE's and the resultant stress have a cumulative effect, especially on the neuro-hormonal, fight or flight system. Time, social support, and a good nights sleep will help recover from stress. Too much unresolved stress leads to post traumatic stress syndrome and aberrant behavior. An individual from a dysfunctional family with few resources has an uphill battle. This at-risk population has already been exposed to more than their share of dysfunctional authority figures and in extreme cases, actual child abuse. Characteristic of this experience is the use of excessive control, distorted guilt, marginalization, and copious punishment. Survivors of these challenging childhoods are all too often mistaken for easy targets for exploitive behavior.

The current cessation programs rely heavily on the use of distorted blame, social ostracization and punishment in the form of job discrimination and exorbitant taxes. The anti-tobacco program forces a choice between two paths, both with negative consequences. It simply produces conflict and adds ....more stress, to those at greatest risk. This unproductive stress increases illness. No study to date has evaluated the extent of this unintended program effect. This thorough analysis needs to be done, especially in the stress sensitive pregnant women (Relier 2001,Meyers 1977) and those exposed to high levels of trauma and stress in the Military/Veteran (Hourani, 1999) populations. Much more effective cessation methods need to be offered, long before health care spends money on programs that appear to continue and institutionalize the dysfunctional relationship that many were exposed to in their youth.

Response:

Although OEHHA is not involved in developing smoking cessation programs, the fact remains that smoking is a big physiological stressor. Active smoking causes both lung and heart disease and is associated with a number of cancers. Smoking cessation is probably one of the best things anyone can do for their health.

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